

# Bilateral temporal tDCS enhances sleep-dependent episodic memory consolidation

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**Introduction:** Human sleep and its role in memory consolidation have been investigated intensively (Born, 2012). It has been found that non-rapid eye movement (NREM) sleep plays a crucial role in hippocampus-dependent declarative memory consolidation (Diekelmann, 2009). In particular, slow waves (SW), which occur mainly during slow wave sleep (SWS), correlate strongly with episodic memory performance (Mander, 2013). While many psychiatric patients suffer from sleep disturbances and memory impairments beside their main symptoms, a possible relation of diminished SWS and memory deterioration has not been sufficiently investigated. In the current proof-of-concept study, we aimed to enhance SW during SWS by inducing weak direct currents with transcranial direct current stimulation (tDCS) to the temporal lobes (including the hippocampi) of healthy participants. Our hypothesis was that increasing the cortical excitability during SWS, sleep-dependent memory consolidation should benefit from tDCS as compared to a placebo condition.

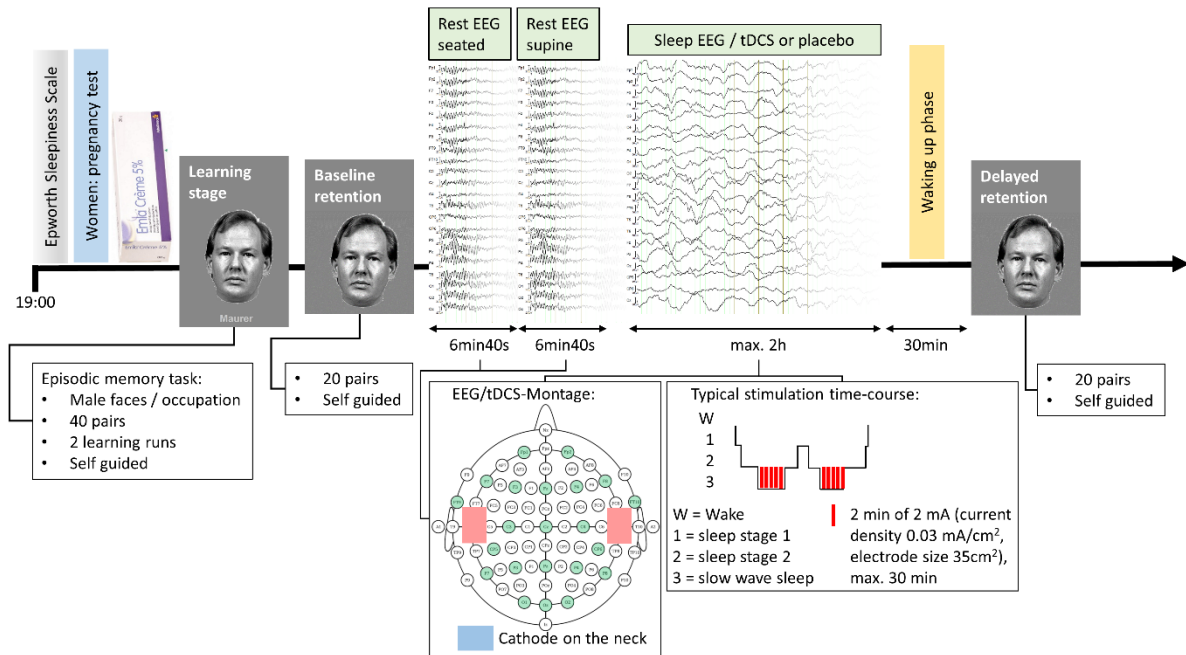
**Methods:** A randomized, placebo-controlled double-blind crossover study design was conducted to apply bi-temporal anodal tDCS (experimental procedure, see Fig. 1). DC with 2 mA (current density 0.03 mA/cm<sup>2</sup>, electrode size 35cm<sup>2</sup> each) was delivered during SWS. Before sleep, participants performed an episodic memory task (face-occupation associations). Memory performance was measured by the number of correctly remembered items (hits). To obtain a value for sleep-dependent memory consolidation, the number of hits at delayed retention were subtracted from the number of hits at baseline. This value was taken to calculate the difference between tDCS and placebo which resulted in the tDCS memory effect. To test if the memory performance was related to the amount of stimulated SW, a partial correlation of the tDCS memory effect coefficient and the amount of SWS during stimulation was computed, with fatigue scores and learning duration as control variables. To this end, a 22-channel EEG was recorded for online sleep-staging and to timely engage the stimulation during SWS. EEG data was preprocessed including ICA, re-referencing to average reference, automatic tDCS-artifact detection, and filtering (0.5-2.0 Hz). Moreover, the data was segmented into 10s epochs that corresponded to clean EEG at SWS after the first stimulation. Finally, SW peak-to-peak amplitudes (> 75  $\mu$ V) were extracted for comparison between tDCS and placebo stimulation.

**Results:** Data of 13 participants (mean age 24, 21-32; 7 females, 6 males) was analyzed. The partial correlation between tDCS memory effect and amount of SWS stimulation showed a strong correlation of  $r = 0.89$  and  $p < 0.01$  ( $df = 5$ ). The same analysis with the amount of SWS placebo stimulation did not reveal any effect ( $r = -0.22$ ,  $df = 7$ ,  $p = 0.56$ ). Focusing on the electrophysiological tDCS effect, there was a moderate increase of SW amplitude in the tDCS compared to the placebo condition (Fig. 2; tDCS:  $M = 93.8$ ,  $SD = 5.7$ ; placebo:  $M = 90.4$ ,  $SD = 6.9$ ;  $T = 2.2$ ,  $p < 0.05$ ).

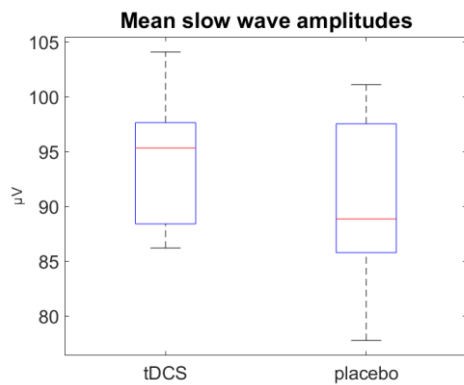
**Discussion:** This study indicates that it is possible to improve sleep-dependent memory consolidation by increasing cortical excitability using tDCS during SWS. Namely, the more SW were stimulated in participants, the better their episodic memory performance. This effect was independent from individual fatigue and learning strategies and was not observed in the placebo condition. Moreover, the increased SW amplitudes in the tDCS condition add electrophysiological evidence of the behavioral tDCS-effect which is in line with our expectations. Yet a few limitations have to be considered. The small sample size leads to a low certainty of the statistical effects. A general issue found in studies using tDCS is the low replication rate. Therefore, replication of the current results is needed in another cohort and also with patients before considering clinical application. Last, an fMRI study would reveal if tDCS increases hippocampal activation as targeted.

## References:

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- Diekelmann, S. et al. (2009), 'The whats and whens of sleep-dependent memory consolidation', *Sleep Medicine Reviews*, vol. 13, no. 5, pp. 309-321.
- Mander, B. A. et al. (2013), 'Prefrontal atrophy, disrupted NREM slow waves and impaired hippocampal-dependent memory in aging', *Nature Neuroscience*, vol. 16, no. 3, pp. 357-364.



**Fig. 1:** Experimental procedure scheme. Red rectangles represent anode tDCS electrodes, blue rectangle represents cathode tDCS electrode. Green shaded EEG electrodes represent recording EEG channels. Each study participant underwent the same procedure twice at least 4 weeks apart, once with tDCS stimulation, and once with placebo stimulation. Memory task stimuli were different for stimulation and placebo conditions.



**Fig. 2:** Boxplot of SW amplitudes averaged after the first stimulation until the end of the recording. SW were defined as oscillations within 0.5 to 2 Hz and larger than 75  $\mu$ V from peak to peak.